II

DIFFICULT PROBLEMS: WHAT SHOULD "A" DO?*

By F. C. DOBLE, M.R.C.S., L.R.C.P.

MR. PRESIDENT, LADIES AND GENTLEMEN,

I appreciate very much the honour you have done me in asking me to open the discussion this evening.

I have been in touch with the speakers who are to follow me, and we have agreed as to the line each shall take; also it seems to us that a discussion should take place after each speaker has finished instead of a combined general discussion at the end.

As these discussions are by far the most important part of this evening's programme, I propose to sketch the outlines of a few difficult problems that have confronted me during the last few years, and I then propose to ask you to comment on them and to raise other queries of the same kind and see if you can find an answer to them. I am afraid I am not offering a prize for the correct solution.

I intend to avoid social problems altogether. Perhaps in the future a paper may be read before this society with some such title as "Social Camouflage in V.D."

I am not going into such questions as regards what to do in the case of the inveterate Wassermann reactor or into the seriological aspect of the subject at all. What I do propose to do is to give very brief notes on a few difficult cases from the point of view of treatment. In some of them I can give you the end results, in others the patients disappeared from my ken without being cured, at any rate by me. All the cases I am going to mention are males.

What should "Dr. A." do to cure these patients?

Amongst the gonorrhœa cases I want to describe two types both fortunately rare.

The first type is one that appears to react well to irrigations of pot. permang. The discharge quickly stops

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and no complication arises, but the moment irrigation is stopped the discharge returns and stops again the moment treatment is resumed. This kind of relapse seems as if it was going on indefinitely.

The second type is still rarer. Irrigations with every known antiseptic or astringent, combined with every other form of treatment, appears to have no effect at all in checking the discharge which pours out day and night. Even after a full overhaul no other complication can be found.

Case No. 1.—A doctor. Acute discharge. Gonococci found in large numbers chiefly extracellular. No treatment had any effect. Was under three specialists at different times. Nine months later was in exactly the same condition. Every known form of treatment was tried. No other complication. Prostate normal.

(End result : Patient was appointed as M.O. to a Fever Hospital. In the first week he got scarlet fever and died.)

Case No. 2.—Invalided from the Rhine. Slight chronic discharge containing gonococci for two and half years. Irrigation with almost every antiseptic stopped the discharge at once, but the patient always relapsed in twenty-four hours after ceasing treatment. The notes on this case showed skilful and varied forms of treatment.

(End result : Cured after two injections of neutralised acriflavine 1 in 5 deep subcutaneously.)

Case No. 3.—A doctor. Chronic gonorrhœa, treated by five or six specialists during three years. One had even put him into a nursing home for protein shock therapy. On several occasions I thought the desired result had been obtained after full dilatations with an anterior Kollmann, but he always relapsed in a few days when irrigations were stopped.

Acriflavine in concentrated solutions and endo- and exo-toxin vaccines failed to cure. Patient disappeared so end result is not known.

Case No. 4.—Same type exactly. Cleared up completely after two intradermal injections of Dimond's vaccine.

Case No. 5.—Very marked hypospadias. I could never find gonococci in the urethra. Patient stated that he was a martyr to gonorrhœa, so I presume that he had had much treatment. Para-urethral ducts going down for $2\frac{1}{2}$ inches, there appeared to be dozens of them, leading

down close to important structures, so they could not be opened up.

(End result : You have probably guessed this by now. Yes, you are quite right. Patience and fused silver nitrate did the trick after some weeks wandering in the catacombs.)

Case No. 6.—Syphilis. Reacted violently to arsenic given in various ways. Bismuth at once caused acute gingivitis. Dentist stated that daily treatment by him was necessary to avoid a serious condition of jaw. Patient very ill. The secondaries which followed a few days after starting treatment rapidly advanced. What should be done to check the disease and save the patient's life ?

Case No. 7.—Syphilis. When first seen patient gave a history of recent acute arsenical dermatitis. Signs of peripheral neuritis. Blood W.R. strongly plus. C.S.F. completely negative. Treatment for nearly three years made the W.R. negative. Aplastic anæmia developed and the patient was taken into a special clinic. Red blood cells were found to be below a million. Transfusion improved the condition. Patient now well on the way to recovery. Expert says that the condition must have been caused by the arsenic, although he owns that he has never seen or heard of a case being caused by it before. Should Dr. A. recommend his patient to continue with injections of arsenic or should he, when the patient has quite recovered, continue with bismuth only ? What say you ?

Discussion

Mr. David Lees remarked that it was difficult to say much with regard to the first case, as the information regarding the cause of death was very indefinite. It was just possible that it may have been due to serum anaphylaxis. So far as the venereal infection was concerned, he appeared to have a poor resistance to it, and it was within the bounds of possibility that he was one of those individuals who had not the power of developing a natural resistance to any infecting agent. In his experience resistant cases of gonorrhœa such as this, in which a discharge recrudesced time after time on ceasing treatment, were not infrequently due to sub-epithelial infiltration of the urethra. In Cases 2, 3 and 4, he should like to know from Major Doble if any attempt had been made

to localise the lesion by urethroscopic examination, by cultures from the prostate and other methods. In patients whose symptoms or signs of infection appeared to subside during irrigation treatment but recrudesced when it was stopped, it was important to try to locate the focus of infection and ascertain whether it was in the prostate gland, the seminal vesicles, or Littre's ducts. In these cases, according to Doble, irrigation of the urethra and bladder had been carried on continuously, and adjuvant treatment had been applied later on by protein shock and exo-toxic vaccines, but only when the former failed to give results. These methods were all very well, but unless the focus of infection was located and drainage established from it, the patient continued infective and the disease in many cases recurred as soon as treatment was stopped. These patients were often the victims of over-irrigation, which led to chemical irritation, and the use of too strong solutions undoubtedly devitalised the tissues. There was much to be said for the policy of leaving well alone and letting the disease become acute again for a time in some of these cases. Many benefited from a holiday and a change of air helped to build up the resistance of the patient. Some cases reacted well to properly spaced doses of vaccine, especially detoxicated vaccine. Some years ago, acting on the principle of Besredka in desensitising horses, he desensitised a series of cases suffering from gonorrhœa by primarily giving a minute dose of detoxicated vaccine intravenously. Two hours after desensitising by this method it was possible to give a potent dose of 20,000 to 50,000 millions of detoxicated vaccine without causing either a local, focal, or general reaction. This method was sometimes successful in a resistant case. In others, again, protein shock by injections of milk or T.A.B. vaccine proved more effective. In his experience, however, none of these methods were likely to prove of value unless the actual focus of infection was located and drained. He cited also a resistant case of gonococcal infection which appeared to be completely cured by the onset of jaundice. It was interesting to note that in patients who were being treated for syphilis concurrently with gonorrhœa, the onset of jaundice almost always ameliorated and often cured the gonococcal infection. In resistant cases occurring in married men, it was of the utmost importance to examine the other partner.

In one case of gonococcal infection in a husband which was said to have lasted for eighteen years, all recurrent attacks of gonorrhœa disappeared subsequent to the excision of a chronic bartholinitis in the female. In Case No. 5, Major Doble had referred to the use of fused silver nitrate in the treatment of littritis. Mr. Lees preferred the electric cautery or instillation into the duct of a liquid preparation of silver nitrate, iodine, or picric acid. He referred to a patient seventy years of age who came under his care some years ago, with a persistent and profuse purulent discharge for three to four weeks, although irrigated two or three times daily. Urethroscopic examination revealed an opening in the roof of the urethra about 1 inch from the meatal orifice which led directly into the space between the layers of the corpus spongiosum, and tracked back to the pouch of Retzius above the pubis. In this case a counter opening in the suprapubic region and the establishment of free drainage cleared up the symptoms of infection in a comparatively short time.

Major DOBLE replied that the man came to Rochester Row and he handed him over to the gonorrhœal section. After he had been there some months he got an appointment as M.O. at a Fever Hospital, and carried on his irrigating. A year later it was learned that he caught scarlet fever, had a high temperature, and died. His death came as a surprise, and it was not thought to be due to nephritis. He appeared to have a marked lack of resistance to disease.

Dr. MILLS suggested that the same sequence might have occurred in this man if he had never had gonorrhœa.

Dr. DOROTHY LOGAN said that in Sheffield in 1917 a V.D. Clinic for women was started, and the conclusion was reached that the onset of gonorrhœa could not be checked. There was then no clinic for men.

Mr. MILLS said that he thought that the explanation of the return of the discharge in certain cases of chronic gonococcal urethritis upon the cessation of irrigation with permanganate, and upon resumption the discharge again stopped, lay in the astringent property of the permanganate. The latter caused the lacunæ to shrink and constricted the apertures of the gland follicles, and, as it were, put a coat of paint over the mucous membrane of the urethra ; hence surface spread of infection from follicle to

follicle was restricted. In gonorrhœa, as in most infections, the institution of free drainage would be an ideal attainment, but unfortunately the anatomy and configuration of the genitalia and their adnexa in the two sexes rendered this impossible in most encysted foci.

In gonorrhœa the patient ultimately cured himself or herself of the infection just as much as did the child with measles, the doctor's efforts being mainly devoted to the prevention of complications. The longer one's experience becomes in dealing with this infection, the more one is impressed with the danger of too much meddlesome treatment from the hands of enthusiasts resulting in a lowering of local, and often general, resistance. One has known of prostates being massaged from the first week of an infection as an example.

By this one does not mean that encysted foci in the urethra, prostate, vesicles, cervix and tubes, should not receive the most thorough and careful surgical attention and treatment, but it is always the patient's own antibodies which kill off the last gonococcus.

He had always felt most strongly that it would be a national asset if a definite research upon gonorrhœa were to be instituted. Treatment in this disease could not be said to have advanced appreciably in the last twenty-five years in comparison with that of syphilis.

Possibly some hope may lay in advances in serum therapy in the future rather than in any local treatments.

Dr. HANSCHELL confessed his dismay on learning from Dr. Doble that incurable gonorrhœa was so peculiar a liability of doctors. He could support Mr. Lees and Mr. Mills in that he, too, had sometimes discovered that by continuing to treat a gonorrhœa patient he had in fact been preventing him from getting well. That was a great nuisance in hospital practice, but in private practice had sometimes had its compensation. He would be chary of prescribing a modern sea voyage. The gonococcus carrier would merely add to the perils of the deep : and certainly the old time sea voyager had brought V.D. to the once happy natives of the Pacific Islands. He agreed with Dr. Dorothy Logan, and would add the corollary that one way of preventing gonorrhœa in men was to cure it in women.

Major DOBLE, in reply, said he chose the cases to narrate which had had every known form of investiga-

tion. The first one was treated by three specialists at Rochester Row, and each hoped he would succeed where the preceding one had failed. Colonel Harrison was called in to see this case.

The man who was on the Rhine brought back very full notes ; he had seen one of the German experts in Cologne. The urethroscope showed the urethra to be normal, as also were the prostate and vesicles. In all the cases he had mentioned there was anterior urethritis, but he did not think the condition extended back to the prostate. Prostatic massage was negative in result.

The first patient realised he was infectious. Case 2 had not a chance : he was a soldier and was in hospital two and a half years. Case 3 had caught gonorrhœa from his wife : he was a doctor and divorced his wife. Case 4 might have been re-infected, but the first three had not been re-infected by the wife or another woman.

He agreed with Dr. Mills' remarks about irrigations with potassium permanganate, but some of the patients had been disappointed with the treatment and had gone elsewhere ; they had not had continuous irrigation during the whole time. The one from the Rhine had not had treatment for three months, he was simply kept in hospital. The urethritis cases were negative under the urethroscope.

The holiday idea was good, but the mental condition of these patients made it difficult for them to take a holiday ; moreover, sending them on a modernly-organised cruise was nowadays risky.

He agreed with what Mr. Lees said about injections in hypospadias ; in that patient there was little penis left ; the openings were like miniature catacombs. He tried to inject a few hundred of them, but the probe caused the openings to dilate, and a week or two later they were gaping, so we knew which had been treated.

Mr. MILLS said that in gonorrhœa it was frequently impossible to be able to exclude absolutely re-infection during the management of a case. In the vast majority of patients the possibility of such was always present. It usually depended entirely upon the truthfulness of the patient, and amongst no unfortunate band of the community did one meet with such a high percentage of liars as in those in the throes of the gonococcus.

Major Doble's soldier, who was said to have been

segregated in hospital for two and half years, might yet have been re-infected. During the War the speaker knew of a case of a soldier in which a similar record of intractability might easily have been chronicled. This man had passed the tests of cure, yet when due for discharge from hospital acquired a bead of pus from a neighbour and inserted it in his meatus, thus perpetuating the disease and his stay in hospital.

Admittedly it was very difficult to say that a woman was not a gonococcal carrier; one might take most careful specimens, employing a suction bougie to the cervical canal after three consecutive menses, and find no gonococci, but yet might find them at the fourth examination. He was therefore very sceptical when informed that a woman who had merely been examined with a speculum could not be a source of infection.

Dr. OSMOND, referring to the para-urethral ducts, said the openings were so tiny and the ducts extended for such an unknown length, that it could scarcely be expected that a solid, a liquid, or a probe would go to the bottom. In some it was possible, by placing a fine pipette in the mouth, to blow them up with air or gas. He asked whether members could suggest a poison gas which, used on gonococci, would exterminate them.

The PRESIDENT said it was unusual to find a patient sensitive to both arsenic and bismuth, and he wondered whether in such a case the kidney condition was a factor. (" There was no kidney trouble.")

Dr. LLOYD asked what was the occupation of the man now being discussed. He might be a worker in metals, and might have been gradually absorbing metallic vapour.

Mr. LEES thought that the mouth condition was not due to bismuth alone and that some septic condition was aggravating and perpetuating the stomatitis. As the patient appeared to be a septicæmic, the condition was probably streptococcal in origin and the therapeutic effect of anti-streptococcal serum might be tried. If the strain of serum happened to be homologous with the infecting agent, excellent results were often obtained. In this case also it was important to drain the focus of sepsis and he doubted if the application of chromic acid would attain this. If the focus of infection were deep-seated the application of strong caustics would not save the patient's life, and he preferred to combine the methods of stimu-

lating the patient's resistance and the attainment of good drainage.

Dr. MORNA RAWLINS thought the condition of the mouth in the case under discussion was due to gingivitis, because the reactions she had had with bismuth had been bad, and the condition cleared up in response to sulphur wash-outs in the mouth.

Dr. SHARP said that in the mouth case the stomatitis might be due to some cause other than the bismuth, such as scurvy or to some blood disease such as leukæmia, of which the enlarged glands, now attributed to syphilis, might be a manifestation. He therefore urged complete blood examination.

The PRESIDENT suggested injections of contramine ; an alternative being the giving of Vitamin " A " in order to raise the resistance against infection. He had never seen reactions in the gums after one or two injections of bismuth. He agreed the condition might have been due to working among metals, and the patient having a susceptibility to a metal.

Major DOBLE (in reply) said the man in question was engaged in choosing chorus girls for the pantomime ! With regard to the Herxheimer reaction, the reaction started within a few minutes of the first injection, whereas the Herxheimer did not show until some days had elapsed. The dental officer had had a large experience, and had seen all kinds of gingivitis. In these conditions arsenic was as much a cause as bismuth. He had an injection of atropine and adrenalin.

The PRESIDENT asked why the dermatitis was thought to be due to arsenic ?

Dr. SHARP said he felt sceptical about the aplastic anæmia, which, if really aplastic, was a fatal condition. He would like to hear more facts about the blood, in addition to the red count. He did not think grave anæmia could be due to ordinary doses of arsenic, as N.A.B. was often given as a treatment for anæmia. This man had been efficiently treated, and he saw no reason for giving more arsenic.

Mr. LLOYD said it was almost certain the case would have progressed rapidly with arsenic and bismuth. He asked whether the patient had earlier received injections of old salvarsan. Many of the cases of aplastic anæmia recorded in literature followed the use of the old sal-

varsan, particularly those reported from the U.S.A. He agreed with Dr. Sharp that cases of real aplastic anæmia were fatal.

Dr. SEMON asked if this was generally considered to be a case of genuine arsenical neuritis. He had always held the view that the evil effects of N.A.B. were the result of poisoning by the benzine radicle and not the arsenic content in the molecule. Considering the enormous number of daily injections given all over the world to-day, it was really astonishing how rarely true arsenical symptoms were reported.

If Major Doble's case was an example of true *arsenical* intolerance it ought to be recorded as such.

Mr. LEES said that he would like to know something more of the bibulous tendencies of this patient. He would not recommend the administration of arsenobenzol to such a patient without some very grave reason. The fact that the man had had three years' treatment with arsenobenzol and bismuth suggested that the dermatitis was not necessarily the result of the injections which he had had. Alcoholic neuritis was a common condition, but neuritis, following up the administration of arsenic and bismuth, was comparatively rare. He remembered one case of neuritis which resulted from excessive dosage of mercury. The patient in question had had 6 grains of grey powder thrice daily for a period of eighteen months without any interval. The neuritis was very marked and was complicated by wrist drop and foot drop. There was no possibility of alcohol in this case, as the patient was confined to a Nursing Home for five or six weeks. Recovery was complete and the patient was subsequently given injections of arsenobenzol without any apparent upset.

In commenting on the case of aplastic anæmia, it was his experience that such cases did not recover. Many, however, were not cases of true aplastic anæmia and were probably cases of severe secondary anæmia. Recently he had seen a case of this type following on bismuth administration. The patient was treated for seronegative syphilis and had never had a postive Wassermann test. During a period of eighteen months a total of 9 grammes of " 914 " and 18 grammes of bismuth metal had been administered. Over a year afterwards this patient was admitted to the medical wards of the hospital suffering from debility,

secondary anæmia, and lumbar pain. With rest in bed and general tonic treatment the symptoms disappeared, but the patient was re-admitted to hospital with the same clinical picture four or five months later. On account of the lumbar pain, radiograms were taken which showed that a depôt of bismuth was still present in the buttocks. It was difficult to prove that the severe secondary anæmia was due to bismuth poisoning, but it was the only evidence which was found to account for the condition. Under the same tonic treatment as previously the patient recovered.

In the case which had been presented to them by Dr. Doble, Mr. Lees was of opinion that the line of treatment should be administration of tonics only ; the serological reactions should be watched carefully from time to time. If further anti-syphilitic treatment were required, a mild bismuth preparation might be administered. As the cerebrospinal fluid gave negative reactions in all tests, there was no indication for intensive treatment. If, in addition, the case had been one of true exfoliative dermatitis, he would have expected the Wassermann test to be negative, as this eventuated in nine cases out of ten who suffered from an exfoliative dermatitis. In most of these cases also the W.R. remained permanently negative.